REMARKS

Applicants wish to thank the Examiner for the courtesy extended during an interview between the Examiner and the Applicants' attorneys wherein possible amendments to overcome prior art rejections were discussed.

Claim 1 has been amended to more clearly point out the claimed invention. Support for the amendment may be found, for e.g., on page 12 (lines 1-10), page 13 (lines 9-11) and page 19 (lines 11-20). Specifically, Claim 1 clarifies that *different* RNAs are being detected, that the substrate is a *microarray* and that the probes are *immobilized* on the substrate. Claims 7-10 are amended. Support for the amendments may be found, for e.g., in Claim 1. New Claims 30 and 31 have been inserted. Support for these may be found, for e.g., on page 35 (lines 1-13) and page 39 (lines 9-12). Claim 20 has been amended to correct a typographical error.

No new matter is presented by the amendments. Applicants do not acquiesce to the propriety of any of the Examiner's rejections nor disclaim any subject matter to which they are entitled by these amendments.

Claim Rejections under 35 U.S.C § 102 should be withdrawn

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. §102 (b) as allegedly being anticipated by Tominaga *et. al.* ("Tominaga"). Applicants respectfully disagree. However, in order to expedite prosecution of the above application, Applicants have amended Claim 1 to recite "hybridizing the sample with a microarray substrate, wherein the substrate has a plurality of different immobilized probes...." etc.

Tominaga discuss a method of detecting alpha globin mRNA transcripts on immobilized-oligonucleotide-coated microtiter plates by reverse transcription with biotinylated mononucleotides. Tominaga use a *single* oligonucleotide (out of four oligonucleotides tested, page 1753, column 1) in order to detect a *single* mRNA species. Our claims teach the use of a *plurality* of *different* probes (oligonucleotides) for the detection of *different* transcripts. The different transcripts may be fragmented from a single parent transcript or a plurality or parent transcripts. Tominaga do not teach detection of a plurality of transcripts/ mRNA species (e.g., results and discussion of RT-PCR and Northern experiments on page 1755).

Because Tominaga do not teach every element of the instant invention, this rejection of Claims 1, 2, 4 and 5 should be withdrawn.

Claim Rejections under 35 U.S.C § 103 should be withdrawn

Claim 3 is rejected under 35 U.S.C § 103(a) as allegedly being unpatentable over Tominaga in view of Takarada *et. al.* ("Takarada"). Takarada teach thermostable RNA dependent polymerase and the Examiner alleges that it would have been *prima facie* obvious to one of ordinary skill in the art to apply Takarada's thermostable enzyme to Tominaga's detection method in order to reverse transcribe the hybridized RNA and increase hybridization and extension specificity. The Advisory Action further alleges that Takarada's teaching of reducing non-specific hybridization would favor Tominaga's probe binding. Applicants respectfully disagree. One of ordinary skill in the art would not be motivated to combine the two references since the detection method taught by the present invention is directed to detecting upstream portions of either the same transcript

or a plurality of transcripts by fragmenting the transcript(s). Tominaga provide neither motivation nor suggestion for analysing *different* RNAs. Therefore this rejection of Claim 3 should be withdrawn.

Claims 6-29 are rejected under 35 U.S.C § 103(a) as allegedly being unpatentable over Tominaga in view of Matson *et. al.* ("Matson"). Matson teach synthesis of oligonucleotides on solid phase in multiwell plates and the Examiner alleges it would allegedly have been *prima facie* obvious to apply Matson's teaching of DNA synthesis on solid support in order to construct a plurality of different oligonucleotides for hybridizing RNA samples in Tominaga's detection method. Applicants respectfully disagree. Neither reference, individually or in combination, suggests the limitation(s) encompassed by the claims of the present invention, particularly, detection of *different* RNAs using *immobilized* probes on a *microarray*. Therefore this rejection of Claims 6-29 should be withdrawn.

In summary, the Examiner has failed to establish a *prima facie* case of obviousness and Applicants respectfully request that the rejection of Claims 3 and 6-29 be withdrawn.

CONCLUSION

Applicants believe the application is now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

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